REMARKS

The claims in this application are 226-239. No fee is believed due but in the event a fee is required, authority is hereby given to charge the same to Deposit Account No. 13-2165.

This application was involved in Interference No. 103,933 which was decided by the Board of Patent Appeals and Interferences in favor of Gregory and adverse to each of Tsui and Collins. That decision was affirmed by the Court of Appeals for the Federal Circuit.

During the course of Interference No. 103,933, a motion under 37 CFR §1.634 to correct inventorship and supporting declarations were filed by Gregory. The Board dismissed the motion as moot and indicated the correction should be addressed in subsequent *ex parte* proceedings.[1] Copies of the relevant documentation are submitted herewith and correction is respectfully requested.

To facilitate the Examiner's review of this application, Applicant briefly summarizes what was determined by the Board with citation to the Board's Decision.

In terms of *benefit*, the Board denied Tsui's motions to deny the benefit of application No. 07/488,307 filed March 5, 1990 for the Gregory claims corresponding to the count in both Interferences Nos. 103,882 and 103,933. The Board thus concurred that Gregory was entitled to such benefit both for the claims corresponding to the count of No. 103,882 (the CFTR cDNA *per se*, that is, the DNA molecule that encodes the cystic fibrosis transmembrane regulator protein) and the claims corresponding to the count in No. 103,933 (directed to a vector comprising (*a*) a regulatory element, and (*b*) the encoding DNA sequence operably linked to the regulatory element).

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[1] It is noted that this amendment is fundamentally one under 37 CFR §1.48(b) in that as a result of amendments or cancellation of claims, fewer than all the currently named inventors is the actual inventor of the invention now being claimed.

With respect to claims directed to the cDNA *per se*, *neither* Tsui nor Collins described how to make CFTR cDNA in any of their commonly claimed earliest applications and thus neither was entitled to the benefit of those applications, namely:

Tsui Applications Failing To Disclose "How To Make" CFTR cDNA	
Appl. No.	Filing Date
07/401,609	Aug 31, 1989
07/399,945	Aug 24, 1989
07/396,894	Aug 22, 1989

The Board thus found that Tsui/Collins encountered problems in making cDNA clones no matter what approach was tried (Board Decision, p.7, ¶ 33).[2]

The Board found Tsui not only failed to disclose the cause of or solution to these cloning problems (Board Decision, p.7, ¶ 34), he did not even acknowledge in his applications that a problem existed with full-length cDNA. (Board Decision, p.10, ¶ 49). Concerning Tsui's representation that the 1989 applications disclosed three partial cDNA clones and that these partial cDNA clones collectively spanned the entire coding sequence, the Board found that Tsui's 1989 application simply did *not disclose how to make* the *full-length* cDNA. (Board Decision, p.7 ¶ 32, AD-8, ¶ 39).

In sum, the Board found Tsui's 1989 applications did not describe how to make the cDNA under 35 U.S.C. § 112, 1st ¶.

Thus while Tsui prevailed in the related Interference No. 103,882 directed to a nucleic acid encoding the CFTR protein, priority was *not* awarded on the basis of an operative disclosure of cDNA prior to Gregory. Rather Tsui prevailed solely on the disclosures of (*i*) genomic DNA and (*ii*) RNA fragments, namely the isolation of an

[2] These problems were well documented in the literature. *See, e.g.,* (*i*) "The Identification of the CF (Cystic Fibrosis) Gene," Plenum Press, New York, 1991, p. 44; (*ii*) Poster Session Abstract, Drumm et al., "The Full Length CFTR cDNA is Toxic in Bacterial Hosts"; (*iii*) Drumm, et al., "Correction of the Cystic Fibrosis Defect In Vitro by Retrovirus-Mediated Gene Transfer," Cell, Vol. 62, 1227-1233 (1990); (*iv*) Strong and Collins, "The Structure of the Cystic Fibrosis Gene," Cystic Fibrosis - Current Topics: Volume I; and (*v*) Tsui, et al., Tsui, "Probing the Basic Defect in Cystic Fibrosis," Current Opinion in Genetics and Development, 1991, 1:4-10.

approximately *250 kb gene* on a 380 kb Sal I restriction fragment (Board Decision, p.6, ¶ 25), and a 6.5 kb RNA from T84 cells that hybridizes with a cDNA probe for CFTR nucleic acids. (Board Decision, p.6, ¶ 26). As has already been noted, however, the Board specifically held that Tsui's benefit applications did *not* disclose how to make the full-length CFTR cDNA.

A count should not be confused with a claim corresponding to that count. It is thus vital to recognize that Tsui's prevailing in interference No. 103,882 does *not* mean Tsui is entitled to a claim to the cDNA. He may be entitled to claims to some genomic DNA sequence on a 380 kb Sal I restriction fragment and/or claims to a 6.5 kb RNA fragment (subject matter the Board found he disclosed) but not a claim to the cDNA (subject matter the Board found he did *not* disclose).

Thus any US patent issuing on Gregory's application, with its March 5, 1990 effective date for the cDNA, would constitute a reference under 35 U.S.C. § 102(e) to any claim by Tsui to the cDNA. Tsui could not remove that reference by reliance on his earlier application (since the Board found Tsui did not disclose the cDNA in compliance with 35 U.S.C. § 112). Similarly, any attempt by Tsui to swear back of Gregory's March 5, 1990 filing date by showing a prior reduction to practice (as for example through use of 37 CFR § 1.131) would be in conflict with the Board's finding that Tsui admitted that as late as April of 1990 he could not produce the cDNA.

It is noted simply for completeness' sake that the Board's decision in the third interference relating to the CFTR protein, No. 104,228, also did not hold that Tsui disclosed a *cDNA* in his 1989 applications. Rather the decision here was based on assertions by Tsui that (*i*) the CFTR protein could be made by injecting *RNA* into *Xenopus* oocytes (Board Decision, p.5, ¶ 22) and (*ii*) CFTR protein could be isolated from the cell membrane fraction of cultured colonic carcinoma cell of the T84 line. (*Id.*, ¶23).

As a consequence of the Board's Decision, as affirmed by the Court of Appeals for the Federal Circuit, *none* of the parties is entitled to claim the cDNA molecule *per se*. Gregory is not entitled to such a claim because of the decision in interference No. 103,882. Tsui is not entitled to the benefit of his three 1989 applications for any claim reading on the cDNA molecule *per se* since he did not disclose how to make a cDNA molecule until *after* Gregory filed.

Tsui's prior applications also are not effective references against the present claims in light of Tsui's admitted inability to prepare a full-length CFTR cDNA. By reasons of prevailing in interference No. 103,933, Gregory thus is uniquely entitled to claim DNA sequences encoding CFTR operably linked to a regulatory element.

In the outstanding Official Action, claims 226 and 227 were rejected on the grounds of double patenting over claims 13-18 of co-pending application No. 08/311,665. Those claims have been cancelled from No. 08/311,665, thus rendering the double patenting rejection moot. Those claims, however, had been indicated previously to be otherwise allowable. Since those claims are not patentably distinct from the present claims and since No. 08/311,665 is a continuation of the present application, with the identical disclosure, the subject matter of the claims 13-18 in No. 08/311,665 has been asserted herein as new claims 228-234.

Thus new claim 228 corresponds substantially to former claim 13 of No. 08/311,665 but has been limited to a host prokaryotic cell. Similarly claim 232 corresponds substantially to former claim 15 of No. 08/311,665.

New claims 229-232 and 233 and 234 are dependent on these claims and further limit these allowable claims. Claim 229 thus depends on claim 228 and specifies that DNA sequence contains at least one silent mutation that stabilizes expression of the gene. Claim 230 claims a plasmid comprising the DNA molecule of claim 228 while claim 231 defines a host prokaryotic cell comprising that plasmid.

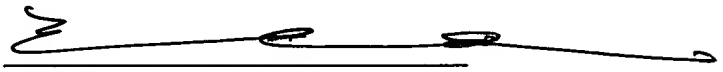
Claim 233 depends on allowable claim 232 and specifies that the regulatory element DNA of the former claim corresponds to at least a portion of the genome of a virus capable of infecting the host cell, while claim 234 specifies the virus is a retrovirus.

New claims 228-234 thus are limited to embodiments defining the same invention as the count of interference No. 103,933.

Similarly, new claims 235-239 correspond to claims 4-6, 17, and 18 of Serial No. 08/470,534, respectively, all of which were therein non-elected and designated as not corresponding to the count in Interference No. 104,228. While a double patenting rejection was not made with respect to Serial No. 08/470,534 (in fact no action following the interference has yet been received in that application), the rationale for the previous restriction therein (in which claims 1, 3, and 7 drawn to CFTR protein compositions were elected) suggest the subject matter of there-non-elected claims 4-6, 17, and 18 should be asserted with the claims of this application.

In view of the foregoing, it is submitted that claims 226-239 are in condition for allowance. The Examiner is invited to contact the undersigned should she believe that this would expedite prosecution of this application.

Respectfully submitted,



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